REMARKS/ARGUMENTS

Claims 107-112, 115, 117, 119, and 120 currently are pending. Claims 1-106, 113, 114, 116, and 118 were canceled previously.

Applicant thanks the Examiner for the withdrawal of the previous rejections of claims 107-112, 115, 117, 119, and 120 under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement and written description support.

Claims 107-112, 115, 117, 119, and 120 have been rejected under 35 U.S.C. § 103(a) as allegedly obvious over Lowe JB[1] (U.S. Patent 5,324,663), Lowe[2] et al. (U.S. Patent 5,770,420), Lowe JB[3] (U.S. Patent 6,268,193), or Sasaki et al. (U.S. Patent 7,094,530), and in view of de Vries et al. (*J. Biol. Chem., 270 (15)*: 8712-8722 (1995)), Seed (International Patent Application Publication WO 96/40881), Staudacher (*Trends Glycosci. Glycobiol., 8 (44)*: 391-408 (1996)), Malissard et al. (*Biochem. Biophys. Res. Commun., 267*: 169-173 (2000)) and Prieels et al. (*J. Biol. Chem., 256 (20)*: 10456-10463 (1981)). The Office Action alleges that the cited references provide ample guidance with respect to all the elements of the present invention and that one skilled in the art could have combined the elements as claimed by known methods and the combination would have yielded nothing more then predictable results. Applicant respectfully traverses this rejection for the reasons set forth below.

For subject matter defined by a claim to be considered obvious, the Office must demonstrate that the differences between the claimed subject matter and the prior art "are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. § 103(a); see also *Graham v. John Deere Co.*, 383 U.S. 1, 148 U.S.P.Q. 459 (1966). The ultimate determination of whether an invention is or is not obvious is based on certain factual inquiries including: (1) the scope and content of the prior art, (2) the level of ordinary skill in the prior art, (3) the differences between the claimed invention and the prior art, and (4) objective evidence of nonobviousness. *Graham*, 383 U.S. at 17-18, 148 U.S.P.Q. at 467.

1. Scope and Content of the Prior Art

The disclosures of Lowe[1], Lowe[2], and Lowe[3] are substantively similar to one another except that Lowe[2] contains an additional example (i.e., Example VII beginning at column 93) not present in Lowe[1] and Lowe[3]. For convenience, discussion of the disclosures of Lowe[1], Lowe[2], and Lowe[3] will be combined and hereinafter referred to as "Lowe," with citations being derived from Lowe[1]. Lowe discloses that extracts from COS-1 cells transfected with DNA encoding human FucT-VI can transfer fucose to an acceptor comprising Galβ1,4GlcNAc or NeuAcα2,3Galβ1,4GlcNAc in an *in vitro* assay (column 89, lines 49-55), and that it may be expected that a catalytically active, secreted protein A-FucT-VI fusion protein which lacks the transmembrane domain of FucT-VI may be generated by fusing amino acids 43 through 359 of FucT-VI (SEQ ID NO:14) to protein A (column 90, lines 9-13). Lowe discloses the activity of FucT-III, FucT-IV, FucT-V, and FucT-VI in transferring fucose to a variety of acceptor substrates, indicating that relative to the efficiency at which each fucosyltransferase transfers fucose to N-acetyllactosamine (i.e., Galβ1,4GlcNAc), FucT-III, FucT-IV, FucT-V, and FucT-VI transfer fucose to α(2,3)sialyllactosamine (i.e., NeuAcα2,3Galβ1,4GlcNAc) at 56%, <1%, 115%, and 110%, respectively (Table 2 following column 92, line 31).

Saskai discloses the cloning of an α-1,3-fucosyltransferase termed "TH21" that is 30-40% homologous to FucT-III, FucT-IV, FucT-V, and FucT-VI at the amino acid level (column 24, line 48 – column 25, line 67, and column 27, lines 6-10). Contrary to Examiner's assertion, Sasaki does not disclose "an isolated polypeptide annotated as FucT-VII" (see pages 11 and 13 of the Office Action). Saskai discloses TH21-IgG (column 45, lines 45-65) and FucT-VI-IgG (column 44, lines 30-40) fusion proteins lacking transmembrane domains which are produced recombinantly in cells as secreted proteins (column 47, lines 20-44). Saskai discloses that the recombinant proteins can be purified and utilized in *in vitro* fucosylation reactions (column 47, line 45 – column 48, line 67).

de Vries discloses the relative fucosyltransferase activity of soluble, protein-A chimeric forms of FucT-III, FucT-IV, and FucT-V, demonstrating that each of the three fucosyltransferases appear to have unique acceptor substrate specificities (page 8713, Table I) and fucose incorporation rates (page 8714, Table II).

Seed discloses the cloning of FucT-VII DNA from a mouse myeloid cell line which may be utilized to generate recombinant FucT-VII polypeptides for the fucosylation of proteins *in vitro* (Abstract, pages 2 and 30, and claim 30).

Staudacher is a review article which discloses that there are at least five different types of human α1,3-fucosyltransferases (i.e., FucT-III, -IV, -V, -VI, and -VII), which are "distinguishable by acceptor specificity, tissue distribution, pH optimum, kinetic properties, cation requirement and sensitivity to inhibitors (Table III)" (page 393).

Malissard discloses that β-1,4-galactosyltransferase I, α-2,6-sialyltransferase, and FucT-VI produced recombinantly in yeast cells display similar kinetic properties as their native counterparts (Abstract).

Prieels discloses two fucosyltransferase activities (i.e., N-acetylglucosaminide α1 → 4 and N-acetylglucosaminide α1 → 3) contained in a single enzyme purified from human milk (Abstract and page 10462, paragraph bridging columns 1 and 2).

2. Level of Ordinary Skill in the Art

For the sake of argument and for purposes of the present analysis, one of ordinary skill in the art can be assumed to be someone with an advanced degree in biochemistry or a similar science and/or several years of experience in the relevant art.

3. Differences Between the Claimed Invention and the Prior Art

Claims 108-112, 115, 117, 119, and 120 depend from claim 107, either directly or indirectly. Claim 107 requires, *inter alia*, an *in vitro* method for modifying the fucosylation pattern of a recombinant glycopeptide comprising contacting a recombinant glycopeptide with a reaction mixture that comprises a fucose donor moiety and a recombinantly produced human FucT-VI or human FucT-VII fucosyltransferase lacking a membrane anchoring domain *wherein said fucosyltransferase provides at least 2-fold greater fucosylation of said glycopeptide than is achieved under identical conditions using recombinant, isolated FucT-V* (emphasis added).

While the Examiner asserts that "the cited prior art provides ample guidance with respect to all the elements of the instant invention" (see page 13 of the Office Action

(emphasis in original)), in fact none of the cited prior art references discloses or suggests a method in which human FucT-VI or FucT-VII provides at least 2-fold greater fucosylation than is achieved with recombinant, isolated FucT-V.

4. Objective Evidence of Nonobviousness

Prior to Applicant's invention, the art had not recognized any substantial difference between the efficiency of fucosylation of the various fucosyltransferases (see page 26, lines 10-11, of the specification). The present invention is based, at least in part, upon Applicant's discovery that certain fucosyltransferases are surprisingly more effective at fucosylating glycopeptides than other fucosyltransferases. As demonstrated in Example 2 of the present application, "[t]he mole fraction of GDP-fucose incorporated into protein was 0.016 for FTV [i.e., FucT-V] and 0.13 for FTVI [i.e., FucT-VI]. Thus, approximately 8-fold more fucose was incorporated using FTVI compared to FTV" (page 44, lines 5-7).

Although several of the cited references disclose that fucosyltransferases display unique substrate specificities (e.g., Table 2 following column 92, line 31 of Lowe[1] and Table III on page 393 of Staudacher), none of the cited references discloses or suggests that FucT-VI or FucT-VII could provide at least 2-fold greater fucosylation than is achieved with recombinant, isolated FucT-V under identical reaction conditions. The only cited reference which compares the amount of fucosylation achieved among different fucosyltransferases under identical conditions is de Vries, which discloses the relative fucosyltransferase activities of soluble, protein-A chimeric forms of *FucT-III, FucT-IV, and FucT-V* (emphasis added). de Vries does not disclose or suggest the use of FucT-VI or FucT-VII, much less provide a comparison of the fucosyltransferase activities of FucT-VI or FucT-VII relative to FucT-V.

Therefore, one of ordinary skill in the art would not have reasonably predicted that FucT-VI or FucT-VII could provide at least 2-fold greater fucosylation than is achieved with recombinant, isolated FucT-V under identical reaction conditions, which is in stark contrast to the Examiner's assertion that "the teachings of de Vries et al., Seed B., Staudacher E., Malissard et al., and Prieels et al., provide guidance for selecting the appropriate fucosyltransferase depending on the experimental need" (see page 11 of the Office Action).

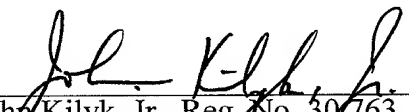
5. Consideration of Graham Factors Together

As recently stated by the Supreme Court, "*there must be some articulated reasoning* with some rational underpinning to support the legal conclusion of obviousness." *KSR Int'l v. Teleflex Inc.*, 550 U.S. 398, 418, 82 U.S.P.Q.2d 1385, 1396 (2007) (quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006) (emphasis added)). Here, the Office has failed to identify a credible reason why one of ordinary skill in the art would modify the fucosylation methods disclosed in the cited references to utilize a different fucosyltransferase as recited in the pending claims. Moreover, the present invention as defined by the pending claims surprisingly provides at least 2-fold greater fucosylation of a glycopeptide than is achieved under identical conditions using recombinant, isolated FucT-V.

Considering all of the Graham factors together, it is clear that the present invention would not have been obvious to one of ordinary skill in the art at the relevant time in view of the cited references. Accordingly, the obviousness rejection of the pending claims should be withdrawn.

Applicants respectfully submit that the patent application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



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